II. REMARKS

This Amendment is being submitted in response to the Office Action dated September 19, 2008 in the above-identified application. Concurrently with this Amendment, Applicant submits a petition for a three-month extension of time for filing a response, along with the requisite fee. Therefore the time for filing a response to the September 19, 2008 Office Action is thereby extended to March 19, 2009, and this Amendment is being timely filed. If it is determined that any additional fee is due in connection with this filing, the Commissioner is authorized to charge said fees to Deposit Account No. 50-0552.

A. Status of the Claims

Claims 1, 2, 4-9, 12, 13 and 15-19 were pending for purposes of the instant Office Action. Claims 3, 10, 11, 14, and 20-42 were previously canceled and claims 7 and 8 were canceled by way of the present Amendment. Accordingly, claims 1-2, 4- 6, 9, 12, 13 and 15-19 remain pending.

Claims 1, 9, 12, 13, and 19 are amended in this Reply. Support for the amendment to claims 1, 13 and 19 may be found in the present specification, for example, on page 6, line 5 to page 7, line 2 and in the original claims 7 and 8, which have now been deleted. Claim 9 was amended to properly claim dependency to claim 1 as claim 8 was canceled by way of the present amendment. Claim 12 was amended to delete a phrase objected to by the Examiner in an attempt to expedite the prosecution of this application. It is respectfully submitted that no new matter was added by virtue of this amendment.

Reconsideration of the application is respectfully requested.

B. Claim Rejections- 35 U.S.C. § 112

Claim 12 was rejected under 35 U.S.C. § 112, second paragraph as being indefinite over the recitation of "wherein the method of pretreating a nucleic acid sample is PCR..." Although Applicants respectfully disagree with the rejection, to expedite prosecution claim 12 has been amended to delete the rejected phrase. Applicants respectfully request reconsideration and withdrawal of the rejection to claim 12 under 35 U.S.C. § 112, second paragraph.

C. Claim Rejections under 35 U.S.C. § 102

Rejection under 35 U.S.C. § 102(b) - Walker (EP 0585660)

Claims 1, 2, 4-9 and 12 stand rejected under 35 U.S.C. § 102(b) as anticipated by Walker (EP 0585660). Claims 7 and 8 have been canceled in the present amendment, and therefore the rejection of claims 7 and 8 is moot. Applicants believe the remainder of the claims are not anticipated by the Walker patent as set forth below.

The Walker patent describes a method of decontaminating the products of a nucleic acid amplification reaction (amplicons) from a nucleic acid sample with exonucleases. See Walker, paragraph [0001].

Claim 1, as amended, recites a method of pretreating a nucleic acid sample obtained from a site and includes the treatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample."

In the Office Action, the Examiner refers to the data from Table 1 of the Walker patent to allege that the Walker patent teaches the addition of contamination nucleic acids (i.e. 1000 amplicons) to the sample and that the claims of the present application are anticipated by the Walker patent. See Office Action, page 4, lines 12 to 15. The disclosure of EP 0585660 is directed to a method to remove single stranded amplicon contamination from prepared nucleic samples. Paragraph [0030] of the Walker patent states:

> "Prior treatment of identical samples actually results in an increase in signals (365000 and 46400 cpm). This signal enhancement probably derives from digestion of the human DNA in the samples. The presence of human DNA results in background amplification which competes with specific amplification of M.tb DNA (Walker et al. (1992), Proc. Natl. Acad. Sci. 89, 392-396)."

The Walker patent describes a method to degrade human genomic DNA in a sample, enabling the decontamination of a mycobacterium DNA and the amplification of target mycobacterium DNA. Circular mycobacterium DNA is not significantly reduced by exonuclease treatments and therefore can be easy decontaminated of foreign DNA. However, the methods described in the Walker patent would be detrimental to the detection and/or removal of amplicon contamination where the DNA profile was determined by the use of single nucleotide polymorphisms as used in forensic studies as per the present application. This is because the conditions required to reliably degrade any contaminating amplicons as described in the Walker patent would also invariably completely degrade any sample nucleic acids, again rendering the determination of a valid DNA profile impossible.

Therefore, the Walker patent teaches away from the present application, as the Walker is concerned with the decontamination of mycobacterium DNA. If the method described in the Walker

patent was used for the purpose of the present invention, the target nucleic acid and the contaminating nucleic acid would both be degraded, rendering the sample useless.

Thus, applicants submit the method of the Walker patent is not suitable to address the problem resolved by the present application. The present application provides a forensic method for removing contaminating nucleic acids, without degrading target nucleic acid for analysis. Claim 1, as amended, recites a method of pretreating a nucleic acid sample obtained from a site comprising the treatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample." The Walker patent does not show or teach the pretreatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample" as recited in claims 1 and 13 of the present invention. Therefore, the Walker patent does not anticipate the claims of the present invention.

As further exemplified on page 4, paragraph 18 of the Walker patent:

"The length of amplicons to be degraded by the method of the present invention will vary depending upon the particular nucleic acid amplification method by which the amplicons are produced, but will usually be at least about 25 nucleotides in length, and typically will be not more than about 2,000 nucleotides in length. When the amplicons are produced by strand displacement amplification, they will typically be not more than about 200 nucleotides in length. Amplicons and target are attacked, but due to the short length of the amplicons and their lack of secondary structure, the amplicons are preferentially cleaved."

As seen from this paragraph, the Walker patent details the preferential cleavage of the small amplicons. Genomic DNA / target nucleic acids, as described in the Walker patent typically comprise nucleic acid fragments of from about 5,000 nucleotides in length to about 200,000 nucleotides in length. See Walker, page 4, paragraph [0017]. Accordingly, a person skilled in the art would know that the Walker patent would not be suitable to address the problem resolved by the present application, as target nucleic acids of forensic interest are often degraded in the method described by Walker. The sizes of the target nucleic acids would commonly be between 200-500bp, which would then be preferentially degraded along with the contaminating nucleic acids; small amplicons. Consequently, the method of the Walker patent cannot be used for the purpose of removing contaminating nucleic acids from samples of forensic value.

Applicants also point out that amended claim 1 adds the phrase "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample." The Walker patent does not show or teach the pretreatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample" as recited in claims 1 and 13 of the present invention and therefore cannot be anticipate the present invention. Specifically, this pretreatment step of contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acids originating from the site and renders them removable from the sample, ensures remaining contaminants as well as the pre-treatment degradation products are effectively removed. Moreover, as shown in Table 1 of the Walker patent, the Walker patent describes a method to remove or inactivate 1000 contaminating laboratory nucleic acids wherein 15 units of exonuclease reduces the signal from 1000 amplicons to essentially the background value of 28,700. See Walker, paragraph [0029] and Table 1. Importantly, the method described in the Walker patent does not effectively remove 10,000 amplicon molecules from equivalent samples (Table 1, page 6), the signal from 10,000 amplicons following treatment with 15 units of exonuclease is 235,000. See Walker, Table 1. Applicants respectfully submit that this result

is not significantly different from the result obtained with the addition of 100 amplicon molecules without exonuclease digestion, indicating that the methods of the Walker patent result only in an approximate 100 fold reduction in contaminating nucleic acids, and the method is not effective in removing large numbers of contaminating amplicons.

In view of the foregoing, the Walker patent does not anticipate the claims of the present invention and withdrawal of the rejection of claim 1under 35 U.S.C. § 102(b) is respectfully requested. Claims 2, 4-6, 9 and 12 depend from claim 1. In view of the foregoing comments to independent claim 1, withdrawal of the rejection of claims 2, 4-6, 9 and 12 under 35 U.S.C. § 102(b) is also respectfully requested.

Rejection under 35 U.S.C. § 102(b) - Miwa (U.S. Patent 4,514,502)

Claims 1-2, 5, 6, 7, 8, 9, 12, 13 and 15 to 19 were rejected under 35 U.S.C. § 102(b) as being anticipated by Miwa (U.S. Patent 4,514,502). Claims 7 and 8 have been canceled in the present amendment, and therefore the rejection of claims 7 and 8 is moot. Applicants believe the remainder of the claims are not anticipated by the Miwa patent as set forth below.

The Miwa patent describes a method for employing RNase I to treat a sample of laboratory-prepared plasmid DNA and removing any contaminating RNA which remains from an earlier bacterial lysis step. See Miwa, col.6, lines 56 - 68 through col. 7, lines 1 - 6 and 48 - 51.

In the Office Action, the Examiner alleges that "in the method of Miwa, the step of treating the nucleic acid sample with RNase constitutes a step of pretreating the sample to remove or inactivate contaminating RNA" as claimed in the present application. See Office Action, page 8, lines 18 to 20.

Applicants respectfully submit that the Miwa patent cannot anticipate because it teaches the use of RNase I at 37°C for the degradation of RNA and does not disclose additional RNases. A person skilled in the art would know that RNAse I is a single stranded RNA only and accordingly, cannot degrade double stranded RNA. Further, a person skilled in the art would know that the application of denaturants to a nucleic acid sample to separate the strands of double stranded RNA would not work, as the enzyme is labile above 37°C and is denatured by most nucleic acid denaturants. Consequently, applicants submit the method taught by the Miwa patent cannot be used to remove all RNA contaminants from a sample and therefore cannot anticipate the claims of the present invention.

Further, the Miwa patent does not teach or suggest a "method of pretreating a nucleic acid sample obtained from a site" as recited in claim 1 of the present invention. The Miwa patent describes the preparation of a plasmid, and there is no reason provided in the Miwa patent for a person skilled in the art to consider the teachings of the Miwa patent for removing contaminating nucleic acids from a site. In contrast, amended claim 1 of the present invention recites "a method of pretreating a nucleic acid sample obtained from a site comprising the steps of: treating the sample prior to analysis to remove or inactivate contaminating nucleic acids purposefully introduced to a site or sample to confound future analysis of target nucleic acids present in the sample that are free or substantially free from other cell components, wherein the treatment is selected from the group comprising of: enzymic treatment, chemical treatment and physical treatment; and contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample." Therefore, the Miwa patent does not teach or show a method of pretreating a sample taken from a site, to remove or inactive contaminating nucleic acids, wherein the contaminating nucleic acid can be RNA as recited in the present invention. Therefore, the Miwa patent does not anticipate the claims of the present invention.

Similarly, the Miwa patent does not disclose the purposeful introduction of contaminating nucleic acids to a site or sample to confound future analysis of target nucleic acids as recited in the present invention.

The Miwa patent also does not show or teach a method of pretreating a nucleic acid sample obtained from a site comprising the treatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample" as recited in independent claims 1 and 13. Similarly, the Miwa patent does not show or teach "treating the sample prior to analysis to remove or inactivate contaminating nucleic acids purposefully introduced to a site or sample to confound future analysis of target nucleic acids present in the sample that are free or substantially free from other cell components, wherein the treatment is selected from the group comprising of: enzymic treatment, chemical treatment and physical treatment" as recited in claim 1 of the present invention.

In view of the foregoing, the Miwa patent does not anticipate claim 1 of the present invention and withdrawal of the rejection of claim 1 under 35 U.S.C. § 102(b) is respectfully requested. Claims 2, 5, 6, 9, 12, 13, 15 to 19 depend, either directly or indirectly, from claim 1. In view of the foregoing comments to independent claim 1, withdrawal of the rejection of claims 2, 5, 6, 9, 12, 13, and 15 to 19 under 35 U.S.C. § 102(b) is also respectfully requested.

Rejection under 35 U.S.C. § 102(b) - Satishchandran (U.S. Patent 6,168,918)

Claims 1, 2, 4-9, 12, 13 and 15 to 19 were rejected under 35 U.S.C. § 102(b) as being anticipated by Satishchandran (U.S. Patent 6,168,918). Claims 7 and 8 have been canceled in the present amendment, and therefore the rejection of claims 7 and 8 is moot. Applicants believe the remainder of the claims are not anticipated by the Satishchandran patent as set forth below.

The Satishchandran patent describes a method of detecting the presence of a plasmid or viral DNA sequence integrated in a chromosomal DNA molecule of a eukaryotic cell in a sample that contains chromosomal DNA molecules of eukaryotic cells and non-integrated foreign DNA, wherein the foreign DNA has at least one DpnI restriction enzyme site as well as one or more non-DpnI restriction enzyme sites which can be cut by non-DpnI restriction enzymes. See Satishchandran, col. 2, lines 15 to 38. Thus, the method of the Satishchandran patent requires the essential step of contaminating DNA to have at least one DpnI restriction site. See Satishchandran, col. 2, lines 28 to 33.

The method of the Satishchandran patent requires a complex number of steps to detect the presence of foreign DNA sequence integrated in a chromosomal DNA molecule. The method requires digestion of the sample, fractionation, an DpnI enzymic reaction, inactivation of the enzymic reaction, digestion of said DNA digestion resulting in fragments, amplification of fragments and detection of amplified fragments. See Satishchandran, col. 2, lines 44 to 62. Claim 1, as amended, recites a method of pretreating a nucleic acid sample obtained from a site comprising the treatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample." The Satishchandran patent does not show or teach a method of pretreating a nucleic acid sample obtained from a site comprising the treatment step of "contacting the sample with a nucleic acid probe that preferentially binds to the contaminating nucleic acid(s) originating from the site and renders them removable from the sample" as recited in independent claims 1 and 13. Therefore, the Satischandran patent does not anticipate the claims of the present invention.

Applicants respectfully submit that the present application addresses the contamination of forensic nucleic acid samples, by other nucleic acids used in forensic DNA profiling. Applicants submits that either nucleic acid samples do not contain relevant Dpn1 sites due to the nature of the

nucleic acid fragment to be decontaminated and tested. Specifically, microsatellite markers, also known as short tandem repeats (STRs), are used in forensic analysis of nucleic acids and/or DNA profiling. Examination of sequences for all of the recognised forensic STRs has demonstrated that none contain DpnI sites. Accordingly, the method described in the Satishchandran patent would not be effective in removing forensic STR contamination.

As noted above, the presence of a restriction site (eg: DpnI) is an essential requirement for the method of the Satishchandran patent. Even if a forensically useful STR had such a site, it would be a simple matter for a criminal to remove the site (whether it is DpnI or another site) without affecting the template in a forensic DNA profiling (PCR) reaction. Consequently, this strategy could not be used to remove contamination from deliberately contaminated forensic samples as proposed in the present application.

In view of the foregoing comments, withdrawal of the rejection of claims 1, 2, 4-9, 12, 13 and 15 to 19, under 35 U.S.C. §102(b), citing Satishchandran, is respectfully requested.

III. CONCLUSION

An early and favorable action on the merits is earnestly solicited.

Respectfully submitted,
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